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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,722	EATON ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.D

DETAILED ACTION

The amendment filed 03/21/2005 has been entered. Claims 1-9, 11-20 are pending and being examined.

Maintained Formal Matters, Objections, and/or Rejections:

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

It is acknowledged that Applicants' deleted the hyperlink on page 18, lines 1-6. However, there is another hyperlink about eight paragraphs later.

Claim Rejections - 35 USC §§ 101, 112

Claims 1-9, 11-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants argue that the data and statements made by Haynes are not compelling because Haynes found that generally increased expression leads to increased protein levels. The examiner does not agree with Applicants' characterization of Haynes because Haynes states:

> These results suggest that even for a population of genes predicted to be relatively homogenous ..., the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript. Page 1863, left column, full paragraph 1.

> "... it is evident that the analysis of mature protein products in cells is essential as there are numerous levels of control of protein synthesis, degradation, processing and

> modification, which are only apparent by direct protein analysis." Page 1863, right column, full paragraph 2.

Therefore, the statements made by Haynes would compel the skilled artisan to question the asserted utilities of the claimed degenerate polynucleotides (the only use of which is in the production of the encoded polypeptide), when the present specification has only provided a differential analysis of PRO3579 mRNA expression.

Applicants argue that Haynes conclusions are based on the analysis of only a small subpopulation of proteins. Applicants' arguments have been fully considered but they are not persuasive. While Haynes conclusions may be based only on the proteins that were detectable, this does not vitiate Haynes finding that among the proteins that were detectable "... the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript" (page 1863, left column, full paragraph 1). Nor does it invalidate Haynes conclusion that:

> The multi-level control of protein synthesis and degradation in cells mean that only the direct analysis of mature protein products can reveal ... their amounts." Page 1870, left column, last full paragraph.

Applicants argue that PRO3579 is not analyzed, mentioned, or taught by Haynes. Applicants' arguments have been fully considered but they are not persuasive. Neither does the present specification analyze PRO3579 polypeptide expression. In fact, the present specification does not provide any information regarding the expression, role, or activity of the PRO3579 polypeptide in cancer.

Applicants argue that Haynes analyzed a yeast genome, not a cancerous mammalian tissue. Applicants' arguments have been fully considered but they are not persuasive. Haynes was cited as providing evidence that protein levels cannot be accurately predicted from mRNA

levels, and that variances as much as 40-fold or even 50-fold were not uncommon (page 1863). Haynes used yeast as an art-accepted model for eukaryotic systems.

Applicants direct the examiner's attention to Kawamoto (Gene. 1996 Sep 26;174(1):151-8) and Yousef (Cancer Res. 2003 May 1;63(9):2223-7). Kawamoto has been considered. Although Kawamoto shows a positive correlation between the abundance of the liver transcript and the protein concentration in the serum, Kawamoto does not know if this correlation holds for proteins that are not secreted into the plasma (page 153, left column, full paragraph 1). The present specification indicates that the PRO3579 polypeptide is a membrane protein, i.e., not a secreted protein, by the presence of the transmembrane domain(s) (Figure 102). In addition, Anderson (Electrophoresis. 1997 Mar-Apr;18(3-4):533-7) reanalyzed the values of Kawamoto and found Kawamoto's higher correlation coefficient to be less convincing because one gene product (albumin) exercises a disproportionate influence on the correlation coefficient. If albumin is omitted from the calculation, the correlation coefficient is reduced to -0.19, which suggest a very poor correlation. See Anderson at page 536, right column, full paragraph 2.

Yousef has been considered. However, Yousef indicates that further experimentation is necessary to establish the usefulness of these KLKs for diagnosis, prognosis, and treatment of ovarian cancer (page 2226, right column, last paragraph). Therefore, Yousef, which discloses more about a potential cancer diagnostic, prognostic, or treatment than the present specification discloses about PRO3579, supports and is consistent with the examiner's position that the present specification fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention,

and that the present disclosure is simply a starting point for further research and investigation into potential practical uses of the claimed polynucleotides.

Applicants argue that Hancock has no bearing on PRO3579 and should not be considered as prior art. Applicants' arguments have been fully considered but they are not persuasive. Hancock is consistent with Haynes. Namely, the analysis of protein products is essential because protein expression levels are not predictable from the mRNA expression levels. One skilled in the art would be required to do further research in order to determine whether or not the PRO3579 polypeptide levels changed significantly in the tumor samples. Such a further research requirement makes it clear that the presently asserted utilities are not yet in currently available form, i.e., they are not substantial.

Applicants argue that Hu does not support the establishment of a baseline of expression data as being correlative with a tumor type because even though a gene that is overexpressed in one type of breast cancer may not be overexpressed in another type of breast cancer, its overexpression would lead the skilled artisan to conclude that the gene is involved in breast cancer. Applicants argue that as long as PRO3579 is overexpressed in one type of melanoma, then this is enough to satisfy the utility requirement. Applicants' arguments have been fully considered but they are not persuasive. In the instant case, the specification provides data showing a qualitative difference in PRO3579 mRNA levels between melanoma tumor and normal skin. PRO3579 mRNA was more highly expressed in melanoma tumor as compared to normal skin. Hu was cited as countervailing evidence to show that the significance of the disclosed analysis of PRO3579 mRNA expression in relation to cancer diagnosis or treatment is unknown. The skilled artisan recognizes that in differential display analysis of mRNA

expression there are biologically relevant results as well as biologically irrelevant results. See Hu (J Proteome Res. 2003 Jul-Aug;2(4):405-12), which teaches that "[h]igh-throughput technologies, such as proteomic screening and DNA micro-arrays, produce vast amounts of data requiring comprehensive analytical methods to decipher the biologically relevant results" (Abstract). "In any microarray experiment, thousands of genes may demonstrate statistically significant expression changes, but only a fraction of these may be relevant to the study" (page 405, left column, full paragraph 1). Therefore, in any microarray experiment there are also biologically irrelevant results and further research is required in order to determine which results are biologically relevant. One skilled in the art would not know if the disclosed PRO3579 mRNA expression is significant or insignificant, relevant or irrelevant. The present specification fails to disclose enough information about PRO3579 mRNA expression to make its usefulness immediately apparent to those familiar with the technological field of the invention.

Applicants argue that Wang is a favorable reflection on the instant data because it supports Applicants' use of mRNA expression as a valid means of facilitating the discovery of novel therapeutic targets in melanoma. Applicants argue that they have done as Wang suggest and that they have met all the factors that Wang suggests. Applicants' arguments have been fully considered but they are not persuasive. The examiner can accept, for arguments sake, that gene expression analysis, tools or techniques have the potential for the discovery of new diagnostic or therapeutic targets. However, one skilled in the art would not know if the disclosed PRO3579 mRNA expression is significant or insignificant, relevant or irrelevant. . The examiner does not agree that such a disclosure provides a "specific benefit in currently available form." This further characterization is part of the act of invention and until it has been

undertaken Applicants' invention is incomplete. The examiner also disagrees with Applicants' assertion that they have met all the factors that Wang suggests because the present specification does not provide any information regarding the target validation of PRO3579 polynucleotide or polypeptide.

Applicants argue that "how much higher" or "how much lower" is not relevant to the issue at hand, nor is it required. Applicants' arguments have been fully considered but they are not persuasive. One skilled in the art would not know if the disclosed PRO3579 mRNA expression is significant or insignificant, relevant or irrelevant. Consequently, the skilled artisan would have a legitimate basis to doubt the utility of the PRO3579 polynucleotide for either cancer diagnosis or treatment.

Applicants argue that PRO3579 is an acyltransferase, citing Brown (1994) and Knutson (1995). However, Brown (1994) and Knutson (1995) are not of record in the present application and the examiner cannot consider evidence that is not of record.

Applicants argue that the mouse homolog of PRO3579 was reported by Cao (J Biol Chem. 2004 Jul 23;279(30):31727-34). Applicant's arguments have been fully considered but they are not persuasive. Cao reports that the murine acyl-CoA:lysocardiolipin acyltransferase 1 (ALCAT1) recognizes both monolysocardiolipin and dilysocardiolipin as substrates with a preference for linoleoyl-CoA and oleoyl-CoA as acyl donors. In contrast, no significant increases in acyltransferase activities by the recombinant ALCAT1 were detected against either glycerol-3-phosphate or a variety of other lysophospholipids as substrates, including lysophosphatidylcholine, lysophosphatidylethanolamine, and lysophosphatidylserine. See the Abstract. Cao also discloses that cardiolipin is the only known dimeric phospholipid, consisting

of four fatty acyl chains, which is restricted to C18 chains dominated by the linoloeyl group (C18:2). The unique fatty acyl composition is believed to be important for its proper biological functions. However, the formation of the unique fatty acyl content of cardiolipin does not occur during de novo biosynthesis, because the enzymes of the cardiolipin biosynthetic pathway lack appropriate substrate selectivity. Hence, newly synthesized cardiolipin is believed to undergo a remodeling process to achieve its appropriate acyl content. See page 31727, right column, full paragraph 1. However, the present specification provides no guidance regarding the substrate specificity or acyl donors of PRO3579. Therefore, simply disclosing "acyltransferase activity" would not reasonably lead the skilled artisan to the unique substrate activity of PRO3579. Cao makes it clear that the asserted "acyltransferase activity" is not yet in currently available form, i.e., it is not substantial.

The present rejection is based upon Applicants' failure to disclose to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. In the present case, the specification does not provide any testing of the level of expression, activity, or role in cancer of the PRO3579 polypeptide. In the absence of this testing and in the presence of evidence, i.e., Haynes and Hu, that protein levels are not always consistent with mRNA levels, and that the significance or relevance of the disclosed PRO3579 mRNA expression in relation to cancer diagnosis or treatment is unknown, the examiner concludes that there is no basis for concluding that the skilled artisan would be convinced that it is more likely than not that the PRO3579 polynucleotide, polypeptide and antibodies could be used for the diagnosis or treatment of cancer.

Applicants' conclusion regarding the utility of the claimed invention has been considered but it is not persuasive. In the present case, the disclosure that DNA68862-2546 is more highly expressed in melanoma tumor as compared to normal skin does not prove that the claimed polynucleotides will perform as cancer diagnostics or therapeutics. The differential expression of the PRO3579 polynucleotide cannot be equated to and has not been adequately correlated with the contemplated cancer diagnostics or therapeutics of the claimed polynucleotides. The claimed polynucleotides have not been tested to the extent that utility would be known to those of skill in the art.

Claims 1-9, 11-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. As Applicants recognize, a rejection under § 112, first paragraph, may be maintained on the same basis as a lack of utility rejection under § 101. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112. Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it. As such, a rejection properly imposed under 35 U.S.C. 101 should be accompanied with a rejection under 35 U.S.C. 112, first paragraph. The 35 U.S.C. 112, first paragraph, rejection set out a separate rejection that incorporates by reference the factual basis and conclusions set forth in the 35 U.S.C. 101 rejection. A 35 U.S.C. 112, first paragraph, rejection

should be imposed or maintained when an appropriate basis exists for imposing a rejection under 35 U.S.C. 101.

Claims 1-9, 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejection of record is applied to claims 11, 12, 13 over how to use the claimed polypeptides having acyltransferase activity.

The examiner construes these claims as if they were directed to or encompassed a nucleic acid molecule encoding a polypeptide having acyltransferase activity.

Applicants argue that the specification discloses how to make PRO3579 variants and that the addition of the functional limitation allows the skilled artisan to make and test the variants for acyltransferase activity. Applicant's arguments have been fully considered but they are not persuasive. As indicated by Applicants, the mouse homolog of PRO3579 was reported by Cao (J Biol Chem. 2004 Jul 23;279(30):31727-34). Cao reports that the murine acyl-CoA:lysocardiolipin acyltransferase 1 (ALCAT1) recognizes both monolysocardiolipin and dilysocardiolipin as substrates with a preference for linoleoyl-CoA and oleoyl-CoA as acyl donors. In contrast, no significant increases in acyltransferase activities by the recombinant ALCAT1 were detected against either glycerol-3-phosphate or a variety of other lysophospholipids as substrates, including lysophosphatidylcholine, lysophosphatidylethanolamine, and lysophosphatidylserine. See the Abstract. Cao also

discloses that cardiolipin is the only known dimeric phospholipid, consisting of four fatty acyl chains, which is restricted to C18 chains dominated by the linoloeyl group (C18:2). The unique fatty acyl composition is believed to be important for its proper biological functions. However, the formation of the unique fatty acyl content of cardiolipin does not occur during de novo biosynthesis, because the enzymes of the cardiolipin biosynthetic pathway lack appropriate substrate selectivity. Hence, newly synthesized cardiolipin is believed to undergo a remodeling process to achieve its appropriate acyl content. See page 31727, right column, full paragraph 1. However, the present specification provides no guidance regarding the substrate specificity or acyl donors of PRO3579. The present specification provides no guidance as to the amino acids in PRO3579 which are important for its catalytic activity, substrate specificity, and structural integrity and which are expendable or substitutable. In the absence of this information a skilled artisan would have to resort a substantial amount of undue experimentation involving random mutation of over 400 amino acid residues, random testing of suitable substrates, and random testing of suitable acyl donors before they could even begin to rationally design a functional nucleic acid molecule encoding a PRO3579 polypeptide having acyltransferase activity. While a specification need not disclose what is well known in the art, that rule does not excuse an applicant from providing a complete disclosure. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. The current claim limitations are analogous to those of claim 7 of U.S. Patent No. 4,703,008, which was held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement in Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 USPQ 2d, 1016 (CAFC, 3/5/91, see page 1026, section D). In that instance a claim to a nucleic acid molecule

encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement. This limitation is analogous to the percent identity and hybridization limitations of the present claims. The disclosure upon which that claim was based described a recombinant DNA encoding EPO and a few analogs thereof. That disclosure differs from the instant specification because, whereas the present specification describes a native PRO3579 cDNA sequence encoding the amino acid sequence of SEQ ID NO:102, it does not describe even a single variant thereof. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. That means disclosing how to make and use enough sequences to justify the grant of the patent protection sought in the present claims. As indicated, the present specification is even more limited than the '008 patent because it describes only a single protein and no analogs or mutants thereof and, therefore, provides even less support than the '008 specification for claims of comparable scope and which were held to be invalid in that patent. Although an Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112, which requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical

elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. It is noted that there is not a single example in the present specification, working or prophetic, of a PRO3579 protein having acyltransferase activity or of a PRO3579 protein whose amino acid sequence deviates from the native sequence of SEQ ID NO: 102. The present specification does not provide a description of a repeatable process of producing a polypeptide having acyltransferase activity, whose sequence deviates from the single disclosed, native PRO3579 sequence. To practice the present invention in a manner consistent with the breadth of the claims would not require just a repetition of work that is described in the present application but a substantial inventive contribution on the part of a practitioner which would involve the determination of the substrate specificity and catalytic activity of PRO3579 and the determination of those amino acid residues in the amino acid sequence of SEQ ID NO: 102 which are required for the functional and structural integrity of that protein. It is this additional characterization of that single disclosed, native protein that is required in order to obtain the functional and structural data needed to permit one to produce a protein which meets both the structural and functional requirements of the present claims that constitutes undue experimentation. In conclusion, the present specification provides no working examples and no guidance that would permit an artisan to practice the invention commensurate with the scope of the present claims. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of

experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claims 1-5, 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection of record is applied to claims 6-9, 11-13 over the lack of a description of polypeptides having acyltransferase activity in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants do not address this rejection in their response filed 03/21/2005. To the extent Applicants may have intended to apply their arguments regarding enablement of the claimed invention to the present rejection, Applicant's arguments have been fully considered but they are not persuasive. Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

In addition and as indicated by Applicants, the mouse homolog of PRO3579 was reported by Cao (J Biol Chem. 2004 Jul 23;279(30):31727-34). Cao reports that the murine acyl-CoA:lysocardiolipin acyltransferase 1 (ALCAT1) recognizes both monolysocardiolipin and dilysocardiolipin as substrates with a preference for linoleoyl-CoA and oleoyl-CoA as acyl

donors. In contrast, no significant increases in acyltransferase activities by the recombinant ALCAT1 were detected against either glycerol-3-phosphate or a variety of other lysophospholipids as substrates, including lysophosphatidylcholine, lysophosphatidylethanolamine, and lysophosphatidylserine. See the Abstract. Cao also discloses that cardiolipin is the only known dimeric phospholipid, consisting of four fatty acyl chains, which is restricted to C18 chains dominated by the linoloeyl group (C18:2). The unique fatty acyl composition is believed to be important for its proper biological functions. However, the formation of the unique fatty acyl content of cardiolipin does not occur during de novo biosynthesis, because the enzymes of the cardiolipin biosynthetic pathway lack appropriate substrate selectivity. Hence, newly synthesized cardiolipin is believed to undergo a remodeling process to achieve its appropriate acyl content. See page 31727, right column, full paragraph 1. However, the present specification does not describe the substrate specificity or acyl donors of PRO3579. Generalized language, such as "acyltransferase activity," does not detail the substrate specificity or acyl donors of PRO3579, and therefore does not describe the acyltransferase activity of PRO3579 because such a disclosure would not reasonably lead those skilled in the art to the particular substrate specificity or acyl donors of PRO3579. Simply describing a large genus of activities, such as "acyltransferase activity," is not sufficient to satisfy the written description requirement as to the particular substrate specificity or acyl donors of PRO3579.

Claim Rejections - 35 USC § 102

Claims 1-9, 11-17 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Applicants argue that the Incyte EST clone no. 2377329 sequence is only 197 bases long. Applicants argue that the novel sequence discovered by Applicants is not covered by the Incyte clone. Applicants argue that the Incyte clone does not provide complete conception of the claimed invention. Applicants argue that conception began with Applicants' bioinformatic techniques, and therefore is not derivation under 35 U.S.C. 102(f). Applicants argue that the full-length sequence could not be derived. Applicants argue that the purchase of a partial clone is not derivation under the intent of 35 U.S.C. 102(f). Applicants argue that conception was not completed by Incyte. Applicant's arguments have been fully considered but they are not persuasive. According to U.S. Provisional application No. 60/172,262:

> the Incyte EST clone no. 2377329 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 1 and is herein designated as DNA68862-2546. Clone UNQ1849 (DNA68862-2546) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 210-212 and ending at the stop codon at nucleotide positions 1452-1454 (Figure 1). The predicted polypeptide precursor is 414 amino acids long (Figure 2).

The only arguable contribution that Applicants make is the identification of the nucleotide sequence of SEQ ID NO: 101 and the characterization of its coding sequence. However, the discovery of properties of a purchased material does not make Applicants the inventor of that material. The identification and characterization of a purchased material also does not make it novel. The purchased material necessarily contains SEQ ID NO: 101, as attested by the fact:

> "the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 1 and is herein designated as DNA68862-2546."

The fact that the Incyte clone necessarily contains SEQ ID NO: 101 and its purchase by Applicants evinces complete conception by Incyte and communication of that conception to

Applicants prior to any date on which it can be shown that Applicants possessed knowledge of the invention.

New Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 1-9, 11-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to or encompass an isolated nucleic acid molecule "wherein said isolated nucleic acid has acyltransferase activity." The specification lacks guidance for making, and working examples of, a nucleic acid molecule having acyltransferase activity. Furthermore, there is no nucleic acid molecule which has been identified in the prior art for which this activity is known and could be extrapolated to SEQ ID NO: 101. In view of the breadth of the claims and the total lack of direction and working examples provided by the inventor, it would require undue experimentation for the skilled artisan to make and/or use the claimed invention.

Claims 1-6, 9, 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims are directed to or encompass a nucleic acid molecule having a recited percent identity to a nucleic acid molecule encoding amino acids 109-353 of SEQ ID NO: 102, or a nucleic acid molecule encoding a polypeptide comprising amino acids 109-353 of SEQ ID NO: 102. The present specification describes an isolated PRO polypeptide, comprising an amino acid sequence having at least about a recited percent identity to an extracellular domain of a transmembrane protein or any other specifically defined fragment of the full-length amino acid sequence (page 8, paragraph 0014). However, the present specification does not specifically define the 109-353 fragment of SEQ ID NO: 102 as either an intracellular domain or an extracellular domain. Figure 102 discloses three transmembrane domains. Thus, the extracellular domain(s) depend on how the polypeptide is arranged in the membrane. Support for the one arrangement implied by the present limitation to the exclusion of the other cannot be found in Figure 102, which raises the issue of new matter.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

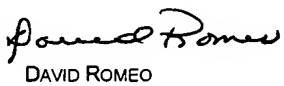
ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JUNE 19, 2005